

AMENDMENT

The following Listing of the Claims will replace all prior versions and all prior listings of the claims in the present application:

Listing of The Claims:

1. (Currently Amended) A method for the selection of a bacteriophage comprising the steps of:

(a) providing a virus comprising a plurality of bacteriophage encoding and displaying a fusion polypeptide, said displayed fusion polypeptide comprising a heterologous polypeptide inserted into the sequence of a bacteriophage coat protein ~~polypeptide~~, wherein said plurality of bacteriophage comprise a sequence specific protease cleavable site located within the displayed polypeptide and which site is protected by folding of the displayed fusion polypeptide and is otherwise either absent from the bacteriophage, or inaccessible to cleavage, or present only in bacteriophage proteins not required after bacteriophage assembly to mediate infection and wherein cleavage of said sequence specific protease cleavable site impairs infection by a said bacteriophage;

(b) exposing the bacteriophage to a protease that recognizes said sequence specific protease cleavable site, wherein said protease only cleaves said sequence specific protease cleavable site if said displayed fusion polypeptide is not properly folded, such that said exposing selects against bacteriophage displaying fusion polypeptide that is not properly folded; and

(c) propagating a bacteriophage comprising intact displayed fusion polypeptide.

2. (Cancelled)

3. (Previously Presented) The method according to claim 1 wherein after exposing said virus to said sequence specific protease, a bacteriophage comprising uncleaved fusion polypeptide is separated from a bacteriophage comprising cleaved fusion polypeptide.
4. (Cancelled)
5. (Currently Amended) The method according to claim 1, wherein the plurality of bacteriophage encode ~~encodes~~ a repertoire of polypeptide sequences.
6. (Cancelled)
7. (Currently amended) The method according to claim ~~any one of claims 5 or 6~~ in which the sequence specific protease cleavable site is comprised within the repertoire of sequences.
8. (Cancelled)
9. (Currently Amended) The method according to claim 1 in which said bacteriophage that is resistant to cleavage displays a folded ~~protein or~~ fusion polypeptide.
10. (Currently Amended) The method of claim 9 in which the cleavage is undertaken under conditions at which some displayed fusion polypeptides ~~members of the repertoire~~ are at least partially unfolded.
11. (Currently Amended) The method of claim 9, wherein the exposing step is undertaken in the presence of a molecule which stabilizes or destabilizes the displayed polypeptide under conditions at which some displayed fusion polypeptides ~~members of the repertoire~~ are at least partially unfolded.
12. (Previously Presented) The method of claim 11, wherein the exposing step is undertaken in the presence of a protein denaturant.

13. (Previously Presented) The method according to claim 1, wherein the exposing step is undertaken in the presence of a ligand for the heterologous polypeptide.
14. (Currently Amended) The method according to claim 1, wherein the method permits isolation of a ~~protein or~~ heterologous polypeptide with improved stability.
15. (Currently Amended) The method according to claim 5, wherein the repertoire of sequences encodes a repertoire of displayed fusion polypeptides ~~proteins~~ which are selected by binding to a ligand.
16. (Cancelled)
17. (Previously Presented) The method according to claim 1 in which the coat protein is that protein encoded by gene 3 of a filamentous bacteriophage.
18. (Previously Presented) The method according to claim 17 in which a cleavage site is introduced between the second and third domain of the gene 3 protein.
19. (Previously Presented) The method according to claim 1 wherein the bacteriophage is a helper bacteriophage used in conjunction with phagemids.
20. (Previously Presented) The method according to claim 19 in which the encapsidated nucleic acid of the helper bacteriophage is a phagemid and requires the use of said helper bacteriophage
21. (Currently Amended) The method according to claim 1, wherein the cleavable site is a sequence specific protease cleavable site, and the cleaving agent is a sequence specific protease selected from the group consisting of trypsin, chymotrypsin, thermolysin, subtilisin, and GLU-C₇, factor XA, Arg C₁, and thrombin .

22. (Previously Presented) The method of claim 1, wherein the sequence specific protease cleavable site is an artificial sequence.

23. (Previously Presented) The method of claim 1, wherein the sequence specific protease cleavable site comprises the sequence of SEQ ID NO: 1.

24. (Previously Presented) The method of claim 23, wherein the sequence specific protease is selected from the group consisting of trypsin, thermolysin, subtilisin, Glu-C, and chymotrypsin.

25. (Previously Presented) The method of claim 1, wherein the heterologous polypeptide is selected from the group consisting of barnase and villin.

26. (Previously Presented) The method of claim 1, wherein the fusion polypeptide further comprises a selectable tag and wherein cleavage removes the tag from the bacteriophage and bacteriophage_comprising the tag are selected.